REMARKS

Pending claims

Claims 1-15 and 54-62 are currently pending in the application. Claims 13 and 15 have been amended for reasons unrelated to patentability. Specifically, claims 13 and 15 have been rewritten in independent form incorporating the subject matter of claim 11. Claims 63-81 are newly presented. Support for these claims is found in the specification and claims as filed at, for example, page 3, lines 33-35; page 6, lines 15-18; page 22 lines 15-19; page 23, line 14-page 24, line 30; page 29, lines 14-29; and page 41, line 16-page 24, line 6.

Restriction Requirement

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Group I. claims 1-2, drawn to isolated protein kinase homologs PKH1-9 classified in class 435, subclass 194.

Group II. claims 3-7, 9, 11-12, 54-62, drawn to isolated polynucleotides encoding said enzymes vectors and hose cell comprising said polynucleotides, methods of expressing said polynucleotides, classified in class 435, subclass 194.

Group III. claim 8, drawn to transgenic organisms comprising said polynucleotides classified in class 435, subclass 194.

Group IV. claim 10, drawn to isolated antibodies which specifically bind said kinases classified in class 350, subclass 387.1.

Group V. claims 13-14, drawn to methods of use of said isolated polynucleotides in hybridization assay, classified in class 435, subclass 6.

Group VI. claim 15, drawn to methods of use of amplifying target polynucleotides, classified in class 435, subclass 6.

In addition to election of one of the inventions I-VI listed above, the Examiner further requested in the 9/12/02 Restriction Requirement that Applicants elect one of the following "inventions":

(A) SEQ ID NO:1, or a DNA sequence encoding it.

(B). SEQ ID NO:2, or a DNA sequence encoding it.

(C). SEQ ID NO:3, or a DNA sequence encoding it.

(D). SEQ ID NO:4, or a DNA sequence encoding it.

(E). SEQ ID NO:5, or a DNA sequence encoding it.

(F). SEQ ID NO:6, or a DNA sequence encoding it.

(G). SEQ ID NO:7, or a DNA sequence encoding it.

(H). SEQ ID NO:8, or a DNA sequence encoding it.

(I). SEQ ID NO:9, or a DNA sequence encoding it.

In response to the first part of the Restriction Requirement, Applicants elect Group IV (original claim 10, now canceled) of which at least newly added claims 63-65, 67, 68, 70, 73-74 and 76-79 fall within the scope of Group IV, with traverse. Further Applicants elect, with traverse, to prosecute invention (E) (SEQ ID NO:5, or a DNA sequence encoding it). Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications. Applicants traverse this Restriction Requirement on several grounds.

Applicants also submit that newly added claims 66, 69, 71, 80, drawn to methods of use of the antibodies of Group IV, and claims 72, 75 and 81, drawn to methods of making the antibodies of Group IV should be examined together with the elected claims. These method claims recite a product (e.g. antibodies) which is of the same scope as the claimed antibodies being searched by the Examiner. Therefore, it would not be an undue burden on the Examiner to examine these method claims since the searches for the claimed antibodies and these method claims would substantially overlap. Additionally, these method claims are entitled to rejoinder upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of a product claim, for rejoinder of process claims covering the same scope of products.

Applicants traverse the restriction of the claims of Group V and Group VI, in that these claims are similar in scope, but not identical to, method of use claims 4 and 5 of parent U.S. Application Serial No. 09/173,581, now U.S. Patent No. 6,013, 455 (the '455 patent) which teach methods of polynucleotide detection. Accordingly, the claims of Group V and Group VI should be examined in view of the following: (1) the fact that the method of use claims (e.g., allowed claims 4 and 5) were not considered separate inventions by the Examiner in the parent application and, (2) the searches that were done on the sequences and methods of allowed claims 1, 4 and 5 in the parent application, examination of claims 13-15 would present a minimal, and certainly not an undue burden on the Examiner. Further, in order to expedite prosecution, and solely for purposes thereof, Applicants would be willing to entertain a request by the Examiner to terminally disclaim any term of allowed claims 13-15 of the instant application to not exceed the term of U.S. Patent No. 6,013,455. For the Examiner's convenience, claims 1, 4-5 of the '455 patent are listed below:

U.S. Patent No. 6,013,455.

1. An isolated and purified polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9.

4. A method for detecting a polynucleotide, the method comprising the steps of:

(a) hybridizing the polynucleotide of claim 3 to at least one nucleic acid in a sample, thereby forming a hybridization complex; and

(b) detecting the hybridization complex wherein said hybridization is performed at 42.degree. C. in a solution containing 250 mM NaCl, 25 mM trisodium citrate,

1% SDS, 50% formamide and 200 .mu.g/ml ssDNA followed by washing at 68.degree. C. in a solution of 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS,

wherein the presence of the hybridization complex correlates with the presence of the polynucleotide in the sample.

5. The method of claim 4, further comprising amplifying the polynucleotide prior to hybridization.

Applicants also traverse the Restriction Requirement as between Groups I and IV drawn to the polypeptides of SEQ ID NO1-9 and the antibodies that specifically bind those polypeptides respectively, in that both (e.g., the polypeptides and the antibodies) could be examined at the same time without undue burden on the Examiner. A search of the prior art to determine novelty of the claims directed to the antibodies would substantially overlap with a search of the claims directed to the polypeptides. Therefore, Applicants submit that examining the prior art for the polypeptides together with that for the antibodies would involve substantially the same subject matter and thus would not impose an undue burden on the Examiner, particularly since the polypeptides have been searched in two previous ancestor applications.

Given that the claimed polypeptides are going to be necessarily searched when searching the claimed antibodies (as discussed *supra*), Applicants also traverse the Restriction Requirement as between Groups I and II (and hence Group IV) drawn to the polypeptides of SEQ ID NO:1-9 and the polynucleotides that encode those polypeptides respectively. Many of the claims of Group II are directed to the polypeptides encoded by the claimed polynucleotides, and thus it is presumed that a proper search for the claimed polynucleotides would include the claimed polypeptides which they encode. Therefore it is submitted that it would not be a substantial burden on the Examiner to use the

results of the necessary polynucleotide search to search the polypeptides as well, particularly since the polypeptides and polynucleotides have been searched together in two previous ancestor applications.

In regard to the election of species of a particular sequence, Applicants traverse on the grounds that the Examiner examined all nine polypeptide sequences (i.e., SEQ ID NO:1-9) in not one, but two ancestor applications: U.S. Application Serial No.'s 09/173,581 and 09/420,915, now U.S. Patent No.'s 6,013,455 and 6,264,947, respectively. Thus, restriction to a single sequence at this time would be unfair as it would contradict the Examiner's positions in the two previous applications that such sequences not be so restricted.

Further according to MPEP §803, a restriction requirement is proper only if (A) the inventions are independent or distinct as claimed, and (B) there would be a serious burden on the Examiner if restriction was not required. Here the restriction requirement is clearly improper given the fact that all nine sequences were examined, and thus searched, in not one, but two previous applications. Thus, the examination of those sequences in the instant application would certainly not present a serious burden on the Examiner.

Applicants also traverse this restriction requirement insofar as it is, in effect, a requirement for election of species as between elements in Markush groups (those elements being, respectively, SEQ ID NO:1-9 with respect to antibodies and the polypeptides to which they specifically bind). The Examiner's attention is directed to the Patent Office's own requirements for Markush practice, set forth in the 8th edition of the M.P.E.P. (August 2001) at § 803.02 regarding restriction requirements in Markush-type claims:PRACTICE RE MARKUSH-TYPE CLAIMS

> If the members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas,* 580 F.2d 461, 198 USPQ 334 (CCPA 1978), **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, **unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.**

This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be

anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. As in the prevailing practice, a second action on the rejected claims would be made final.

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a *non-elected species,* the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry. [emphasis added]

As can be seen from the above, the present Restriction Requirement does not meet the Patent Office's own requirements. First and foremost, if the number of "members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. **In such a case, the examiner will not follow the procedure described below and will not require restriction**." Withdrawal of the restriction requirement as between the nine specific sequences each in the claims is required on that basis alone. Corroboration for the fact that the nine sequences are indeed sufficiently few in number or so closely related, all being protein kinases, that a search and examination of the entire claim can be

made without serious burden is found in the fact that the Examiner has already examined all nine sequences in two ancestor applications.

Second, **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. Broadly, **unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility**." Clearly, the antibodies of the present invention share a common utility, for example, detection of a disease associated with the expression the polypeptides of SEQ ID NO:1-9. They also share a substantial structural feature in that the polypeptides to which they specifically bind, SEQ ID NO:1-9, are protein kinases.

Third, even if the claims could be considered to be "Markush-type generic claims which include a plurality of alternatively usable substances or members," it is further noted that the M.P.E.P states that "A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, "**the examiner may require a provisional election of a single species** prior to examination on the merits" but if no prior art is found, examination must continue on the other claimed species. This clearly applies in the present case.

Therefore, it is respectfully submitted that, upon searching and examining the antibodies which specifically bind to the polypeptides related to SEQ ID NO:5, and finding no prior art over which they can be rejected, the Examiner **must** extend the search of the Markush-type claim to include the non-elected species.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 10 and 16-53 have been canceled.

Claims 13, 15 have been amended as follows:

13. (Once Amended) A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of [a polynucleotide of claim 11] a polynucleotide selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:10-18,

b) a naturally occurring polynucleotide comprising a polynucleotide sequence at least 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:10-18,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d),

the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

14. A method of claim 13, wherein the probe comprises at least 60 contiguous nucleotides.

15. (Once Amended) A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of [a polynucleotide of claim 11] a polynucleotide selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:10-18,

b) a naturally occurring polynucleotide comprising a polynucleotide sequence at least 90%identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:10-18,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d),

the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

New claims 63-81 have been added as follows:

63. (New) An isolated antibody which specifically binds to a polypeptide selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence of SEQ ID NO:1-9,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1-9, said naturally occurring amino acid sequence having protein kinase activity, and

c) an immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO:1-9.

64. (New) The antibody of claim 63 which specifically binds to a polypeptide comprising an amino acid sequence of SEQ ID NO:1-9.

65. (New) The antibody of claim 63 which specifically binds to a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to an amino acid sequence of SEQ ID NO:1-9, said naturally occurring amino acid sequence having protein kinase activity.

66. (New) A diagnostic test for a condition or disease associated with the expression of PKH in a biological sample, the method comprising:

a) combining the biological sample with an antibody of claim 63, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex, and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

67. (New) The antibody of claim 63, wherein the antibody is:

a) a chimeric antibody,

b) a single chain antibody,

c) a Fab fragment,

d) a $F(ab')_2$ fragment, or

e) a humanized antibody.

68. (New) A composition comprising an antibody of claim 63 and an acceptable excipient.

69. (New) A method of diagnosing a condition or disease associated with the expression of PKH in a subject, comprising administering to said subject an effective amount of the composition of claim 68.

70. (New) A composition of claim 68, wherein the antibody is labeled.

71. (New) A method of diagnosing a condition or disease associated with the expression of PKH in a subject, comprising administering to said subject an effective amount of the composition of claim 70.

72. (New) A method of preparing a polyclonal antibody with the specificity of the antibody of claim 63, the method comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence of SEQ ID NO:1-9 or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibodies from said animal, and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid sequence of SEQ ID NO:1-9.

73. (New) A polyclonal antibody produced by a method of claim 72.

74. (New) A composition comprising the polyclonal antibody of claim 73 and a suitable carrier.

75. (New) A method of making a monoclonal antibody with the specificity of the antibody of claim 63, the method comprising:

a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO:1-9 or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibody producing cells from the animal,

c) screening the isolated antibodies with the polypeptide, thereby identifying a monoclonal antibody which binds specifically to a polypeptide having an amino acid sequence of SEQ ID NO:1-9.

76. (New) A monoclonal antibody produced by a method of claim 75.

77. (New) A composition comprising the monoclonal antibody of claim 76 and a suitable carrier.

78. (New) The antibody of claim 63, wherein the antibody is produced by screening a Fab expression library.

79. (New) The antibody of claim 63, wherein the antibody is produced by screening a recombinant immunoglobulin library.

80. (New) A method of detecting a polypeptide having an amino acid sequence of SEQ ID NO:1-9 in a sample, the method comprising:

a) incubating the antibody of claim 63 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence of SEQ ID NO:1-9 in the sample.

81. (New) A method of purifying a polypeptide having an amino acid sequence of SEQ ID NO:1-9 from a sample, the method comprising:

a) incubating the antibody of claim 63 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) separating the antibody from the sample and obtaining the purified polypeptide having an amino acid sequence of SEQ ID NO:1-9.